

IN THE CLAIMS

1-13. (Canceled)

14. (Original) A method for diagnosing an aggressive tumor phenotype comprising:

- (i) contacting a tumor tissue sample with oligonucleotides which recognize PBR RNA;
- (ii) detecting the presence or absence of a duplex formed between PBR RNA in said sample and oligonucleotides specific therefor;
- (iii) and comparing it to the amount of duplex formed in a normal tissue sample, wherein an increase in duplex in the suspected tissue over normal indicates the presence of an aggressive tumor phenotype.

15-29. (Canceled)

30. (Original) A method for detecting the level of PBR in cells using the polymerase chain reaction said method comprising:

- (i) extracting RNA from a sample;
- (ii) reverse transcribing said RNA into cDNA
- (ii) contacting said cDNA with
 - (a) at least four nucleotide triphosphates,
 - (b) a primer that hybridizes to PBR cDNA,

and

- (c) an enzyme with polynucleotide synthetic activity,

under conditions suitable for the hybridization and extension of said first primer by said enzyme, whereby a first DNA product is synthesized with said DNA as a template therefor, such that a duplex molecule is formed;

- (iii) denaturing said duplex to release said first DNA product from said DNA;
- (iv) contacting said first DNA product with a reaction mixture comprising:
 - (a) at least four nucleotide triphosphates,
 - (b) a second primer that hybridizes to said first DNA, and

(c) an enzyme with polynucleotide synthetic activity,
under conditions suitable for the hybridization and extension of said second primer by
said enzyme, whereby a second DNA product is synthesized with said first DNA as a template
therefor, such that a duplex molecule is formed;

(v) denaturing said second DNA product from said first DNA product;

(vi) repeating steps iii-vi for a sufficient number of times to achieve linear production of
said first and second DNA products;

(vii) fractionating said first and second DNA products generated from said PBR cDNA;
and

(viii) comparing the level of PBR cDNA with the level of PBR cDNA from a normal
cell;

wherein, an increase in PBR level over normal cells indicates an aggressive tumor phenotype.

31. (Original) A method for determining the aggressive phenotype of a tumor cell
detecting PBR RNA in said cell and comparing the level of PBR RNA to the level of PBR RNA
from a normal cell wherein an increase over normal in PBR RNA in the tumor cell indicates an
aggressive tumor phenotype.

32-36. (Canceled)

37. (Previously Presented) A method to detect the presence of a variant peripheral-type
benzodiazepine receptor (PBR) gene in a physiological sample, comprising: determining whether
RNA obtained from a physiological sample encodes a variant PBR with a substitution at codon
147 or at codon 162.

38. (Previously Presented) The method of claim 37 comprising (i) extracting RNA from
the sample; (ii) subjecting the RNA to conditions that result in a duplex DNA molecule
corresponding to the RNA; (iii) amplifying at least a portion of the duplex DNA to achieve linear
production of amplified DNA; (iv) determining whether the amplified DNA encodes a variant

PBR with a substitution at codon 147 or at codon 162.

39. (Previously Presented) The method of claim 37 wherein the sample is a tumor biopsy.

40. (Previously Presented) The method of claim 37 wherein the sample is a breast tumor biopsy.

41. (Previously Presented) The method of claim 37 wherein the sample is a colon cancer biopsy.

42. (Previously Presented) A method to detect the relative level of variant PBR RNA in a sample, comprising hybridizing a probe specific for variant PBR RNA and a probe specific for wild-type PBR RNA to a sample comprising nucleic acid; comparing level of variant PBR RNA to level of wild-type PBR RNA and thereby determining the relative level of variant PBR RNA in the sample.

43. (Previously Presented) The method of claim 37 or 42 which employs *in situ* hybridization.

44. (Previously Presented) The method of claim 37 or 42 which employs Northern hybridization.

45. (Previously Presented) The method of claim 37 or 42 which employs polymerase chain reaction.

46. (Previously Presented) The method of claim 42 wherein the probe for the variant PBR RNA detects a codon for arginine at position 162.

47. (Previously Presented) The method of claim 42 wherein the probe for the variant PBR

RNA detects a codon for threonine at position 147.

48. (Previously Presented) The method of claim 42 wherein the probe is about 20 to about 50 nucleotides in length.

49. (Previously Presented) The method of claim 37 or 42 wherein the variant PBR RNA corresponds to a sequence as set forth in SEQ ID NO:1 or SEQ ID NO:2.